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Case Report

Bilateral Eyelid Ptosis, Attributed to Vincristine, Treated Successfully with Pyridoxine and Thiamine in a Child with Acute Lymphoblastic Leukemia

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ABSTRACT

Vincristine-induced neurotoxicity is an adverse effect commonly seen in pediatric patients treated for cancer. We hereby present a case of a 6-year-old boy with acute lymphoblastic leukemia, who developed bilateral eyelid ptosis 25 days after the last intravenous administration of vincristine (cumulative dose 14.2 mg i.e., 17.75 mg/m^2). The boy was treated with 5 mg/kg thiamine and with 10 mg/kg pyridoxine. Complete recovery of ptosis was noticed 4 weeks after the initiation of Vitamins B1 and B6 supplementation therapy.

Key words: Neurotoxicity, ptosis, vincristine, Vitamin B1, Vitamin B6

INTRODUCTION

Vincristine-induced neurotoxicity is an adverse effect commonly seen in pediatric patients treated for cancer.[1] Impaired microtubule function involved in axonal transport can lead to varying degrees of sensorimotor neuropathy in approximately half of the patients.[2] Therapeutic protocols for children, however, have not been established, as detailed studies on them are lacking.

CASE REPORT

We hereby present the case of a 6-year-old boy with high-risk acute lymphoblastic leukemia, who developed bilateral eyelid ptosis, 25 days after the last intravenous administration of vincristine (according to ALL IC-BFM 2009 Protocol II, which includes two doses of 1.5 mg/m^2/day each, on days 1 and 6). The patient recovered fully after pyridoxine and thiamine treatment. Normal nerve conduction studies, normal magnetic resonance imaging (MRI) of the brain, and normal cerebrospinal fluid (CSF) findings, pointed to the diagnosis of vincristine-induced peripheral neuropathy.

Our patient developed drooping of both upper eyelids (moderate ptosis of 3–4 mm, with a levator function of 5–10 mm), with no other accompanying symptoms during the chemotherapy course mentioned above [Figure 1]. Blood and CSF tests, along with brain MRI, revealed no pathology. Antibodies for acetylcholine were not detected in the boy's serum. Fundoscopy was normal while visual acuity examination of the patient produced a result of 6/9 using Kay pictures. Decreased

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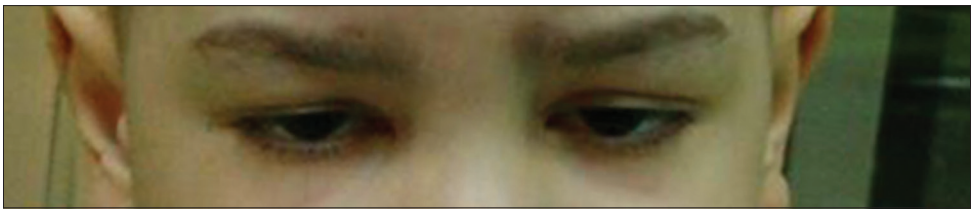


Figure 1: Bilateral ptosis before treatment

ability of both eyes to move upward was also recorded by a pediatric ophthalmologist. Examination by the pediatric neurologist revealed defected horizontal eye movement to the right side, but with normal findings in the rest of the physical. Electromyoneurography studies were conducted twice during the course of the present disease, and both showed no indication of polyneuropathy. In addition, the boy was malnourished in the days prior to the manifestation of ptosis (with undernutrition and severe electrolyte disorders as hypokalemia). Based on the young patient's history, we concluded that the cause was vincristine-induced neurotoxicity, and the boy was treated with 5 mg/kg thiamine mononitrate (100 mg once daily per os) and with 10 mg/kg pyridoxine hydrochloride (200 mg once daily per os). Complete recovery of ptosis was noticed 4 weeks after the initiation of Vitamins B1 and B6 supplementation therapy [Figure 2].



Figure 2: Complete recovery of ptosis after 4 weeks of treatment

DISCUSSION

Several chemotherapeutic agents such as taxanes, platinum analogs, vinca alkaloids, bortezomib, and thalidomide are related to neurotoxicity (with an incidence ranging from 3% to 13%). Pathogenetically, vinca alkaloids (like vincristine), bind tubulin, and by inhibiting microtubule dynamics, they cause irreversible damage to the mitotic spindle. Peripheral neuropathy is observed when the cumulative dose of vincristine administered exceeds 6 mg/m^2.[3] In our case, the patient received 14.2 mg of vincristine (17.75 mg/m^2) adhering to the protocols' instructions. Other risk factors, such as previously reported hypersensitivity to vinca alkaloids, severe malnutrition, liver dysfunction, preexisting neurological disorder, and the use of other neurotoxic drugs, including allopurinol, erythromycin, isoniazid, mitomycin C, phenytoin and itraconazole, seem to correlate with higher incidence of toxicity.[1] Notably, our patient had no other risk factors, except malnutrition, for developing neuropathy. The clinician should be aware of the fact that malnutrition alone can lead to myopathies.[4] Discontinuation of chemotherapy in combination with oral administration of Vitamins B1 and B6 also seem to have a positive outcome in mild cases of vincristine-induced neuropathy, comparable to formerly published data suggesting treatment with pyridostigmine.[5,6] Nonetheless, contraindications of pyridostigmine in cases of mechanical intestinal, or urinary obstruction, and bronchial asthma should be always taken into account.

CONCLUSION

Ultimately, even though the administration of Vitamins B1 and B6 seems to promote complete recovery of bilateral ptosis, further research is required to valorize this finding and determine the neurological monitoring of vincristine administration. Furthermore, the prompt detection of ptosis is crucial, as it is usually fully reversible in early stages.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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